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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/287,332	04/07/1999	KAARE M. GAUTVIK	16777/309	6190

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FOLEY AND LARDNER
3000 K STREET NW SUITE 500
WASHINGTON, DC 200075109

EXAMINER

LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 11/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/287,332

Applicant(s)

GAUTVIK ET AL.

Examiner

Robert Landsman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 October 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38,39,41 and 57-59 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38,39,41 and 57-59 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/28/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Formal Matters

- A. The Amendment dated 10/28/04 has been entered into the record.
- B. Claims 38, 39, 41 and 57-59 are pending and are the subject of this Office Action.
- C. The Information Disclosure Statement dated 10/28/04 appears to have two pages to the Form 1449. However, only page one, references A1-A8 could be found.
- D. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Specification

- A. The specification is objected to since it appears that Applicants have not provided Sequence Identifiers (SEQ ID NOs) for the signal sequences disclosed on page 25, lines 10, 18 and 26. According to 37 CFR 1.821(d) (MPEP § 2422), where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

3. Claim Objections

- A. Claims 37, 38, 41 and 57-59 are objected to since the term "cell free" should be hyphenated.

4. Double Patenting

- A. Applicants requested that the double patenting rejection over co-pending application 08/340,664 be held in abeyance until the present application is in condition for allowance. This request has been granted.

5. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

- A. The rejection of claims 38, 39, 41 and 57-59 under 35 USC 112, first paragraph, has been withdrawn in view of the fact that the claims are drawn toward "medium" and not towards methods of making the PTH protein. Therefore, while the claims may be rejected under 35 USC 102 and 103, the claims appear enabled as worded for simply obtaining medium containing secreted PTH.

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6. Claim Rejections - 35 USC § 112, first paragraph – new matter

A. Claims 38, 39, 41 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 38 recites “said PTH fraction does not contain chemically modified amino acids.” Applicants have not identified where in the specification support for this limitation can be found. **This is a new matter rejection.**

7. Claim Rejections - 35 USC § 112, second paragraph

A. Claims 38, 39, 41 and 57-59 are rejected under 35 USC 112, second paragraph, since the metes and bounds of “chemically modified” in claim 38 are unknown. This term is not defined in the specification.

8. Claim Rejections - 35 USC § 102

A. Claims 38, 39, 41 and 57-59 remain rejected under 35 USC 102 as being anticipated by Breyel et al. for the reasons already of record on page 4 of the Office Action dated 2/27/04. Applicants argue that the PTH of Breyel was obtained by lysing the cells via sonication and that because the cells of Breyel et al. were lysed the resulting extract contains most of the soluble molecules of the cells, including proteases. They, therefore, argue the presence of such proteases during expression and purification of a recombinant protein is undesirable because such proteases would degrade the protein of interest. Applicants argue that, in contrast to Breyel, the PTH of the present invention is secreted in the medium and is, therefore, not degraded.

These arguments have been considered, but are not deemed persuasive. Regardless of the fact that the cells of Breyel were lysed, this does not mean that the PTH was degraded. It is well-known in the art that in order to keep cells viable the medium needs to be changed on a regular basis. Therefore, the discarded medium, which would have been discarded before the cells were lysed, would have contained intact PTH. Furthermore, as seen on the second page of Breyel, under “Detection of PTH activity in bacterial extracts,” the authors removed and sonicated only a 1ml aliquot of a 50 ml solution of cells. Therefore, 49 ml of cell culture medium remained and was not sonicated. It would be expected, therefore, that PTH, which is normally secreted into the medium, would be present, undegraded, in the 49 ml of “unused” culture. The medium of Breyel would not be expected to contain any chemically modified

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amino acids, especially in absence of the definition of "chemically modified." IT would be expected that any "biological modifications" by the bacteria would not be considered "chemical modifications."

B. Claims 38, 39, 41 and 57-59 remain rejected under 35 USC 102 as being anticipated by Applicants' specification for the reasons already of record on page 5 of the Office Action dated 2/27/04. Applicants submitted a Declaration by Dr. Kaare Gautvik under 37 CFR 1.132 as requested by the Examiner under 37 CFR 1.105. The Declaration states that the PTH standard has been modified and is not identical to that of the PTH of the present invention. The Declaration is persuasive in demonstrating that the PTH of the invention is different from that of the standard. However, this rejection is being maintained since the specification has not provided a definition of the phrase "chemically modified." It would be expected that certain groups would be modified upon synthesis in E. coli and yeast.

9. Claim Rejections - 35 USC § 103

A. Claims 38, 39, 41 and 57-59 remain rejected under 35 USC 103 for the reasons already of record on pages 5-6 of the Office Action dated 2/27/04. Applicants argue that the PTH of Breyel or Mayer contained significant fragments since E. coli contains endopeptidases and exopeptidases, whereas Brewer does not contain fragments since it was obtained from dried, defatted parathyroid tissue. Furthermore, purification would be difficult due to the fragments present in the sample. Finally, Applicants argue that the protein of Breyel is not mature.

These arguments have been considered, but are not deemed persuasive. First, the claims recite that the PTH fraction consists essentially of intact PTH(1-84). However, there is no definition of this term in the specification. Therefore, in the absence of this definition, the PTH fraction of Breyel or Mayer would also consist essentially of fragments of PTH.

The other major concern raised by the Examiner is that nowhere in the claims are the endopeptidases and exopeptidases removed from the cells/medium. Applicants' invention is performed in E. coli which, according to Applicants' arguments, contains these enzymes. Therefore, it would be expected that the cell-free medium would contain these enzymes in the absence of any method step to eliminate them. Therefore, one skilled in the art would expect the medium to contain PTH fragments. Furthermore, enzymes are not 100% efficient and are saturable. Therefore, it would be expected that even in the presence of peptidases in Breyel or Mayer some PTH would remain intact. Again, in the absence of a definition of "essentially of," the limitations of the present claims have been met.

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A concern, therefore, is raised in that if the peptidases are not removed or inactivated, how the present invention is enabled, according to Applicants' arguments. The only difference the Examiner can identify which distinguishes the PTH from the prior art is that the present invention uses a "double start codon." However, this requirement is not present in the claims, nor does this procedure appear to be well-established in the prior art. Therefore, it is still not clear how the claimed medium is distinguished over the prior art.

10. Conclusion

A. No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on M-Th 9 AM-6 PM (eastern); alt F 9 AM-6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert Landsman
Primary Examiner
Art Unit 1647


ROBERT LANDSMAN
PATENT EXAMINER